

## Unexpected Diagnosis of Schizophrenia in Young Woman with Severe form of Rheumatoid Arthritis

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### Abstract

### Case Report

Schizophrenia and rheumatoid arthritis are chronic conditions that seem to have little in common. Their association is very rarely reported. However, different studies have shown a common genetic ground for these two diseases at the origin of a reduced risk of occurrence of rheumatoid arthritis in schizophrenic patients and vice versa. We report the exceptional case of a 35-year-old woman followed, over a period of seven years, for seropositive rheumatoid arthritis complicated by joint deformities and pulmonary involvement. The patient has been on corticosteroids and Plaquenil for 7 years. The patient presented behavioral disturbances with delusional seizures two years ago and received neuroleptic medication. The patient was admitted for marked clinical deterioration, joint deformities and stiffness, pressure ulcers in the sacral region and bilateral pleurisy. We also note the presence of behavioral disorders requiring a psychiatric view which noted the presence of a dissociative syndrome associated with an autistic syndrome and a delusional syndrome. Blood tests showed an important biological inflammatory syndrome. Autoantibodies for other autoimmune diseases were negative. Viral and bacterial serologies were negative. Brain MRI was normal. The diagnosis of schizophrenia was established and treatment with neuroleptic was started. Currently, the patient has a problem with managing her RA due to poor adherence to her treatment, the existence of serious complications and the absence of active communication.

**Keywords:** Arthritis, Rheumatoid; Schizophrenia ; Case Reports; Epidemiology; HLA Antigens.

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## INTRODUCTION

Rheumatoid arthritis (RA) is a common autoimmune disease and schizophrenia (SZ) is a relatively common neurological disorder. Both diseases have a chronic course. Their etiology remains unknown [1]. Both disorders evolve into relapses-remissions course and their diagnosis is syndromic and is based on a set of clinical and paraclinical criteria [2]. There is no specific diagnostic test for either of the two pathologies [2].

The relationship between SZ and RA is particularly interesting because of a reduced prevalence of RA in schizophrenic patients [1]. In fact, the prevalence of the two pathologies seems to have a negative correlation: RA decreases in schizophrenic subjects compared to the general population and vice versa [1, 3]. If the similarities between these two pathologies seem unlikely, the inverse correlation of their respective prevalence has intrigued several researchers. Hypotheses of diagnostic underestimation in schizophrenic patients were put forward at the beginning, then other research theories made it possible

to evaluate metabolic, biochemical, immunological, infectious and genetic mechanisms which would be at the origin of this epidemiological finding [2, 3]. Finally, several publications have reported a common genetic origin involving a negative association of these two diseases [1, 2]. Therefore, the association between SZ and RA has been reported very exceptionally. We present here a rare case of SZ appeared on ground of RA.

## CASE REPORT

We report the observation of a 35-year-old woman who has been followed for 7 years for seropositive RA. Verbal consent, for the publication of the data of this observation, was obtained by the young woman's parents.

RA appeared one month after childbirth. Currently, the patient has severe complications such as joint deformities and pulmonary involvement. She has been treated with corticosteroids and plaquenil for seven years then she stopped these treatments without any medical advice 2 months ago. Two years ago, the

patient presented 2 behavioral disorders. In fact, episodes of hallucinatory voices giving a running commentary on the patient's behaviour, breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms and acute delirium attacks were found. In addition, sleep disturbances and negative symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses resulting in social withdrawal have also been reported. No information concerning the examinations initially carried out was given. Neuroleptic medication was started but she stopped it without medical approval. Currently, the patient is admitted to the rheumatology department for aggravation of RA with significant anorexia and weight loss. She also presents articular deformities and stiffness, dry ocular-oral syndrome, pressure ulcers in the sacral region and bilateral pleuritis. On examination, the patient also had behavioral problems that required a psychiatric opinion that revealed the presence of a dissociative syndrome associated with an autistic syndrome and a delusional syndrome (delirium of persecution and bewitchment, whisper-like auditory hallucinations). Biological tests revealed a biological inflammatory syndrome, an elevated level of rheumatoid factor in both serum and pleural fluid. Autoantibodies of other autoimmune diseases were tested negative including anti-nuclear antibodies, extractable nuclear antigen antibodies, anti-neutrophil cytoplasmic antibodies and anti-transglutaminase antibodies. Neither additional viral nor bacterial infections were found. Brain magnetic resonance imaging did not reveal any abnormalities that could explain these psychiatric disorders. The diagnosis of SZ was made according to DSM V criteria for SZ. Therefore, neuroleptic medication was initiated. Currently we have a problem managing this patient's disease because of her poor compliance with medication, the existence of serious complications (rheumatoid pleuropulmonary disease, urinary tract infections, gastroduodenitis, pressure ulcers) and the absence of active communication.

## DISCUSSION

RA is a chronic inflammatory disorder that mainly affects small joints: RA is described as a bilateral, symmetrical, erosive, destructive and deforming lesion of small joints [4, 5]. SZ is a psychiatric disorder characterized by delusions, hallucinations, disorganized speech and disorganized behavior [6]. RA and SZ are two nosologic entities that are different at first sight, but a long-standing epidemiological enigma is the reduced prevalence of RA in patients with SZ and their families [7, 8]. In the literature, the authors reported the negative correlation between the prevalence of RA and schizophrenia [9]. Indeed, several studies have found that the risk of RA in SZ patients is 29% lower than in the general population [10]. Failure to report somatic disorders in people with schizophrenia would be a contributing factor, but the

prevalence of RA is not reduced in people with other psychiatric disorders [7].

SZ and RA look very different on first assessment. However, further analysis reveals some common features. Clinically, these diseases have a chronic evolution on a relapsing and remitting course [1, 2].

On the epidemiological side, SZ and RA have a similar estimated prevalences : 0.46% for RA and 0.6% for SZ [7, 8]. In addition, both conditions have an increased mortality [9]. However, there are also differences, including the age of onset (16 to 30 years in SZ vs 25 to 55 years in RA) and the male: female ratio (nearly 3 women to 1 man for RA and 1 woman for 1.4 men for the SZ) [11]. The study of established risk factors for RA has shown a reduced prevalence of this pathology in schizophrenic patients despite a high prevalence of smoking subjects in this population [12].

Several pathophysiological hypotheses have been investigated to try to explain this protective SZ-RA interaction [11], such as an abnormal metabolism of tryptophan [13], prostaglandin deficiency [14], corticosteroid imbalance [15], psychosocial factors [11] or therapeutic consequences [10]. No evidence has been provided to support these hypotheses [9].

Furthermore, other pathogenic mechanisms appear to be potentially probable in both diseases, such as factors involving immune activation, including infectious agents. History of infection with viruses such as the Epstein-Barr virus and the *Toxoplasma gondii* parasite has been found in SZ and RA [2]. SZ is a neural developmental disorder that can be induced by immune activation in early life secondary to perinatal risk factors such as infection and early term of birth [16-18]. RA is an autoimmune disease while SZ has a very likely autoimmune component [19]. The autoimmune hypothesis of SZ is supported by epidemiological evidence showing a higher risk of autoimmune disorders in SZ compared to controls despite the negative relationship between SZ and RA being negative [20].

Moreover, SZ and RA involve a genetic etiological component. The hereditary family character is estimated at 40% for RA and 64% for SZ [21, 22]. In RA patients, this heredity is expressed more extensively in seropositive RA [23-25]. The negative correlation of their respective prevalence would be genetic in origin with mutations leading to the development of RA and protecting against schizophrenia. A team has identified variants of single nucleotide polymorphism that could explain the significant genetic associations between schizophrenia and rheumatoid arthritis. These mononucleotide polymorphisms are located only in the HLA region, in particular at the level of HLA-B and HLA-C [7, 26].

This observation illustrates, in addition to the originality of the SZ and RA association, the difficulty of the management of a patient who developed serious complications following an iterative abandonment of her treatments and a lack of cooperation secondary to her schizophrenia.

## CONCLUSION

Further investigations should be carried out in this patient in order to understand the potential factors having induced the existence of a very improbable association and very particularly the genetic characteristics.

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Verbal consent, for the publication of the data of this observation, was obtained by the parents of the young woman.

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